

## **EXAMPLE OF REPLACEMENT OF SUBJECTS**

The replacement of subjects is protocol specific and needs to be tailored to the trial.

### **Example:**

If a subject is withdrawn from the dose escalation cohort for any reason other than a dose limiting toxicity (DLT) prior to completing the first 28 days of [Agent X] treatment, a replacement subject will be enrolled and will be assigned to the same dose level.

If a subject is withdrawn from cohort(s) appropriate #(s) (dose expansion) prior to the week appropriate # assessments (in particular DCE-MRI), a replacement subject may be enrolled as agreed upon by the sponsor and the investigators.

### **Example:**

**If Oral Drug is to be taken 21 out of 21 days and this is not met:**

If a subject does not take at least 17 doses in the first cycle, the subject will be replaced because he/she has not taken enough drug to confirm safety at that dose level.

### **Example:**

**If subject does not receive a certain percentage of doses:**

Subject will be replaced if they do not receive 75% of planned doses of [Agent X]